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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,096	02/14/2002	Keiichi Sato	033808/0282094	1424

7590

11/13/2003

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EXAMINER

SISSON, BRADLEY L

ART UNIT PAPER NUMBER

1634

DATE MAILED: 11/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/077,096	Applicant(s) SATO ET AL.	
	Examiner Bradley L. Sisson	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 October 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 4-11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 4-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

### *Specification*

1. The amendment filed 29 October 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

- That text which was added to page 5, paragraph 3, as the specification as originally filed did not identify where the incorporated material was found in Japanese Patent No. 2756474.
- Claim 1, line 3, which reads in part: “having exclusively freely mobile sample biopolymers therein.

Acknowledgement is made where applicant, at page 6 of the response of 29 October 2003, directs attention to page 4, last paragraph; page 1, line 18, and page 1, lines 10-11, as providing support for “a sample biopolymer solution having **exclusively** freely mobile sample biopolymers therein” and that the at least one probe biopolymer hybridizes with “**freely mobile sample biopolymers**” (emphasis in the original). A review of the cited passages fails to locate support for the new claim language. It would appear that applicant is attempting to satisfy the requirement of prior support through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43

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USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at

1966:

Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

2. Applicant is required to cancel the new matter in the reply to this Office Action.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Attention is directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a “written description of the invention” which is separate and distinct from the enablement requirement. The purpose of the “written description” requirement is broader than to merely explain how to “make and use”; the “applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the “written description” inquiry, *whatever is now claimed*.

For convenience, claims 1 and 7, the only independent claims, are reproduced below.

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1. (Currently Amended) A sheet for covering a substrate ~~[[hybridization device]]~~ comprising ~~[[a sheet having a]]~~ at least one hydrophilic surface region containing a sample biopolymer solution having exclusively freely mobile sample biopolymers therein and a hydrophobic surface region surrounding the hydrophilic region, wherein the substrate is fixed with at least one probe biopolymer to hybridize with the freely mobile sample biopolymers in the sample biopolymer solution when the hydrophilic surface region faeing contacting a probe-biopolymer-fixed region of [[a]] the substrate when the sheet and the probe-biopolymer-fixed substrate are arranged in layers.
7. (Currently Amended) A hybridization device, comprising a substrate fixed with ~~[[a probe]]~~ at least one biopolymer in a probe-biopolymer-fixed region and ~~[[the]]~~ a sheet ~~[[of claim 1]]~~ for covering the substrate, said sheet having at least one hydrophilic surface region containing a sample biopolymer solution therein and a hydrophobic surface region surrounding the hydrophilic region, wherein said probe biopolymer hybridizes with the sample biopolymer when the hydrophilic surface region contacting the probe-biopolymer-fixed region.

For purposes of examination, the claim 1, and claims 2 and 4-6, which depend therefrom, have been interpreted as encompassing a "sheet" of virtually any thickness, and of virtually any length and depth. A review of the disclosure, however, fails to find an adequate written description of such a sheet. It is noted with particularity that page 3, last line, states:

The thickness of the sheet 2 is about 1 mm.

The specification has been found to only teach that the sheet and substrate are of the dimensions of a glass slide. In support of this position, attention is directed to page 3, last paragraph, bridging to page 4 of the specification, which for convenience, are reproduced below.

Figure 1 is a schematic view showing a structure of a hybridization device according Embodiment 1 of the present invention. A silicone-rubber-based sheet 2 has a hydrophilic region 3 and a hydrophobic region 4. The hydrophilic region 3 is a region that faces a DNA-fixed (generally biopolymer-fixed) region of a substrate (not shown) and the hydrophobic region 4 is a surface region of the sheet 2 surrounding the hydrophilic region 3. The thickness of the sheet 2 is about 1 mm. The substrate on which the probe biopolymers are fixed is made of glass, plastic, metal or the like. The dimensions of the slide glass commonly used as the substrate is 76 x 26 mm<sup>2</sup> according to the Japanese standard, 3 x 1 inch<sup>2</sup> (25.4 mm<sup>2</sup>) according to the American standard, and 25 x 75 mm<sup>2</sup> according to the European standard. Silicone rubber is generally hydrophobic and glass is hydrophilic.

Accordingly, the specification does not reasonably support the position that applicant possessed sheets of virtually any dimension (or devices that comprised same).

4. It would appear that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

5. Applicant is urged to consider narrowing the claims to those embodiments that are adequately described in the original disclosure.

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6. Claims 1, 2, and 4-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, e.g., *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

7. A review of the specification fails to find where any starting materials and reaction conditions have been set forth such that one of skill in the art could practice the claimed invention to the full extent of the claims' scope without having to resort to undue experimentation. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

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“ ‘[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.’ *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) (‘[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.’).

\*\*\*\*\*

“Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that ‘a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.’) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

“It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

8. The claimed device clearly relates to performing nucleic acid hybridization reactions as well as performing amplification reactions (e.g., PCR). Both of such technologies are recognized in the art as being problematic and require greater levels of enabling disclosure. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

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In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

In support of this position, attention is directed to the following teachings. Zhang et al.,

*Bioinformatics*, Vol. 19, No. 1, 2003, page 14, states:

It is widely recognized that the hybridization process is prone to errors and that the future of DNA sequencing by hybridization is predicated on the ability to successfully cope with such errors. However, the occurrence of hybridization errors results in the computational difficulty of the reconstruction of DNA sequencing by hybridization. The reconstruction problem of DNA sequencing by hybridization with errors is a strongly NP-hard problem. So far the problem has not been solved well.

Chan (US Patent Application Publication US 2002/0119455 A1):

[0018] In practice, Probe Up methods have been used to generate sequences of about 100 base pairs. Imperfect hybridization has led to difficulties in generating adequate sequence. Error in hybridization is amplified many times. A 1% error rate reduces the maximum length that can be sequenced by at least 10%. Thus if 1% of 65,536 oligonucleotides gave false positive hybridization signals when hybridizing to a 200-mer DNA target, 75% of the scored "hybridizations" would be false (Bains, 1997). Sequence determination would be impossible in such an instance. The conclusion is that hybridization must be extremely effective in order to generate reasonable data. Furthermore, sequencing by hybridization also encounters problems when there are repeats in sequences that are one base less than the length of the probe. When such sequences are present, multiple possible sequences are compatible with the hybridization data. (Emphasis added.)

As set forth in Carrico, (US Patent 5,200,313) the extent and specificity of hybridization is

affected by the following principal conditions:

- The purity of the nucleic acid preparation.

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- Base compositions of the probe - G-C base pairs will exhibit greater thermal stability than A-T or A-U base pairs. Thus, hybridizations involving higher G-C content will be stable at higher temperatures.
- Length of homologous base sequences- any short sequence of bases (e.g., less than 6 bases), has a high degree of probability of being present in many nucleic acids. Thus, little or no specificity can be attained in hybridizations involving such short sequences. From a practical standpoint, a homologous probe sequence will often be between 300 and 1000 nucleotides.
- Ionic strength- the rate of reannealing increases as the ionic strength of the incubation solution increases. Thermal stability of hybrids also increases.
- Incubation temperature- Optimal reannealing occurs at a temperature about 25 - 30 °C below the melting temperature for a given duplex. Incubation at temperatures significantly below the optimum allows less related base sequences to hybridize.
- Nucleic acid concentration and incubation time- Normally, to drive the reaction towards hybridization, one of the hybridizable sample nucleic acid or probe nucleic acid will be present in excess, usually 100 fold excess or greater.
- Denaturing reagents- the presence of hydrogen bond-disrupting agents, such as formaldehyde and urea, increases the stringency of hybridization.
- Incubation- the longer the incubation time, the more complete will be the hybridization.
- Volume exclusion agents- the presence of these agents, as exemplified by dextran and dextran sulfate, are thought to increase the effective concentrations of the hybridizing elements thereby increasing the rate of resulting hybridizations.

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- Further, subjecting the resultant hybridization product to repeated washes or rinses in heated solutions will remove non-hybridized probe. The use of solutions of decreasing ionic strength, and increasing temperature, e.g., 0.1X SSC for 30 minutes at 65 °C, will, with increasing effectiveness, remove non-fully complementary hybridization products.

9. As presently worded, the sheet and device are to both comprise a sample solution. The specification has not been found to set forth a reproducible procedure whereby any target nucleic acid sequence can hybridize to probes while in the continual presence of the “sample biopolymer solution.”

10. In view of the breadth of scope claimed, the limited guidance provided, the unpredictable nature of the art to which the claimed invention is directed, and in the absence of convincing evidence to the contrary, the claims are deemed non-enabled by the disclosure. Accordingly, claims 3-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Response to arguments

At page 5 of the response received 29 October 2003, it is asserted:

**second paragraph, as being indefinite. The claims are being amended either according to the Examiner’s suggestion or to be enabled by the specification by reciting the corresponding US application of JP. Pat. No. 2756474. Accordingly, the withdrawal of the outstanding formal objections is in order, and is therefore respectfully solicited.**

The above argument has been fully considered and has not been found persuasive as the amendment to the specification in and of its self introduces new matter into the disclosure, which 1) needs to be deleted and 2) cannot be relied upon. Assuming *arguendo*, that the material introduced does not constitute new matter, the material incorporated does not enable the making

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and use of the claimed device. The specification, with or without the incorporated subject matter does not set forth reaction conditions under which the claimed sheet and device are to be used. Such non-disclosure unfairly shifts the burden of enablement from applicant to the public. See *Genentech v. Novo Nordisk A/S*.

11. For the above reasons and in the absence of convincing evidence to the contrary, the rejection is maintained.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1, 2 and 4-11 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 1 and 4-11 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the specification originally filed. At page 2, applicant has stated:

The hybridization device of the invention comprises a sheet having a hollowed region and a region surrounding the hollowed region, the hollowed region facing a probe-biopolymer-fixed region of a substrate when the sheet and the probe-biopolymer-fixed substrate are arranged in layers.

This statement indicates that the invention is different from what is defined in the claim(s) because the invention of claim 1 is no longer a “hybridization device,” but a sheet, and that the sheet lacks the requisite hollowed region. The “hybridization device” of claims 7 and 9-11 lacks the requisite “hollowed region.”

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14. The sheet of claims 1, 2, and 4-6; and the hybridization device of claims 7-11 do not recite the limitation that the hollowed region faces “a probe-biopolymer-fixed region of a substrate when the sheet and the probe-biopolymer-fixed substrate are arranged in layers.”

### *Conclusion*

15. Rejections that appeared in the prior Office action and which were not repeated hereinabove have been withdrawn.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

17. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

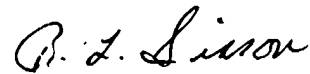
18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978.

The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

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19. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

20. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bradley L. Sisson  
Primary Examiner  
Art Unit 1634

BLS  
November 12, 2003